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10/524,044

12/12/2005

Laurent Meijer

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23117 7590 09/29/2009  
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EXAMINER

PIHONAK, SARAH

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

09/29/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/524,044 | <b>Applicant(s)</b><br>MEIJER ET AL. |  |
|                              | <b>Examiner</b><br>SARAH PIHONAK     | <b>Art Unit</b><br>1617              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 June 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 10-39 and 41-46 is/are pending in the application.
- 4a) Of the above claim(s) 34-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10-33, 38, 39 and 41-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This application is a 371 (national stage application) of PCT/EP03/09515, filed on 8/8/2003.

#### ***Priority***

This application, filed on 12/12/2005, claims foreign priority to Application No. 02292019.3, filed on 8/9/2002.

#### ***Response to Arguments***

1. In the office action dated 12/23/2008, claims 1-12, 14-20, 22, 23, 25, 26, 28-32, and 38-43 were rejected under 35 USC § 112, second paragraph, for being indefinite. In the response filed on 6/22/2009, the Applicant had amended the drawing of chemical formula I for claim 1, to comply with a standard chemical structure. However, it is noted that the amended drawing for formula (I), of claim 1, is still indefinite, for the following reasons: the ring structure has a ring position 7, which is not defined by the claim, and there are two positions denoted as position "2" on the ring structure. Therefore, as the ring position "7" is not defined, and it is not certain which position Applicant intended to denote as position "2", claim 1 is indefinite, and the rejection of this claim under 35 USC § 112, second paragraph, is maintained. Claims 2-4 and 38-43, as well as new claims 44-46, which are dependent claims of claim 1, are also rejected. For Applicants' convenience, this rejection will be restated further in this office action. The rejection of claims 5-12, 14-20, 22, 23, 25, 26, and 28-32, which have been amended to be limited to a compound of formula (II), is withdrawn.

The drawings had previously been objected to for not having a description of the drawings present in the specification. In the amendment filed on 6/22/2009, the Applicant submitted a description of the drawings; therefore this objection is withdrawn. Claims 16-20, 23, 25, 26, and 28-32 were previously rejected under 35 USC § 112, second paragraph, for not defining the substituent R in formula (I). The claims have been amended as dependent claims of claim 5, which includes a structure of formula (II) with R present. The rejection of these claims is therefore withdrawn due to the amendment.

Claims 42 and 43 were previously rejected under 35 USC § 112, second paragraph, for being indefinite. The claims have been amended to remove the terms "preferably 300 to 600 mg". The rejection of these claims is withdrawn due to the amendment.

Claims 39 and 40 were previously rejected under 35 USC § 112, first paragraph, for lack of enablement. Claim 39 has been amended to remove the terms "preventing neurodegenerative disorders", and claim 40 has been cancelled. Therefore, the rejection of these claims is withdrawn.

Claims 1-12, 14-20, 22, 23, 25, 26, 28-32, and 38-43 were previously rejected under 35 USC § 102(e) as being anticipated by Picard et. al., US 6,943,174 patent. In the response filed on 6/22/2009, the claims were amended; the rejection of these claims under 35 USC § 102(e) over Picard et. al., in view of the amendments, is withdrawn. Claims 8-9 and 40 have been cancelled, and claims 44-46 have been added. However, in further consideration of the claims, a new rejection under 35 USC § 103(a), and a

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new rejection for obviousness-type double patenting, has been made, which will be explained in depth further in this office action. Accordingly, due to the new grounds of rejection, this action is made **NON-FINAL**.

As stated in the previous office action, the elected compound of formula (I), compound 39, has been found to be free of the prior art. Therefore, the search was expanded to additional compounds of formula (I). Claims 13, 21, 24, 27, and 33-37 were previously withdrawn due to the election of species requirement. However, the search was expanded in this office action to include claims 13, 21, 24, 27, and 33, which are similar structurally. Claims 34-37 remain withdrawn, as they are directed to compounds that have different core structures and non-elected inventions.

2. Claims 1-7, 10-23, 24, 25, 26, 27, 28-32, 33, 38-39, and 41-46 were examined.
3. Claims 1-7, 10-23, 24, 25, 26, 27, 28-32, 33, 38-39, and 41-46 are rejected.

#### ***Claim Rejections-Obviousness Type Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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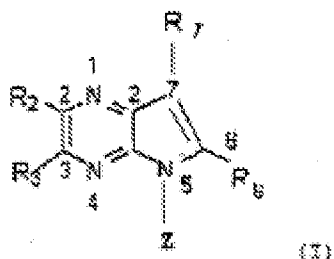
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-7, 10-23, 24, 25, 26, 27, 28-32, 33, 38-39, and 41-46 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-40 of copending Application No. 11/665294. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to compositions comprising the same compounds.

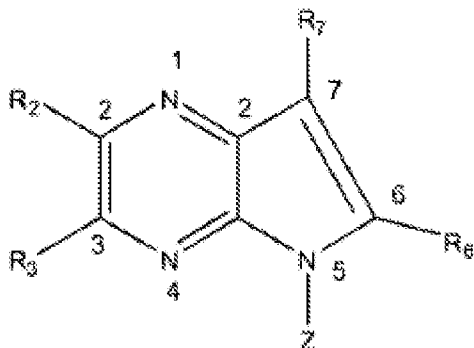
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are directed to compounds of formula (I) below:



Where R<sup>7</sup>=H, alkyl, etc.; Z=CH<sub>3</sub>; R<sub>6</sub>=optionally substituted aromatic cyclic group or cycloalkyl group. The substituent "7" on the ring, while not defined by claim 1, is further defined by dependent claims as carbon. The instant claims are also directed to pharmaceutical compositions comprising a carrier, administered in various forms, in dosages from 100 to 1000 mg.

The co-pending claims are drawn to compositions comprising compounds of formula (I), shown below, in pharmaceutical carriers for administration in various forms:



Where  $R^2$ ,  $R^3$ =H, etc.;  $R^6$ =optionally substituted aromatic ring, or cycloalkyl, etc.;  
 $Z$ =CH<sub>3</sub>, etc.;  $R^7$ =H, alkyl, etc. It is noted that the instant claims are drawn to compounds and compositions for treating Alzheimer's disease, while the co-pending claims are drawn to compositions for treating cystic fibrosis. However, these are composition claims, and not methods of treatment. Therefore, such language drawn to treatment in composition claims is intended use, which is not given patentable weight. Additionally, the composition claims include routes of administration and dosages; as the claims are drawn to a composition, and not a method of treating, language drawn to administration and dosages is intended use, and is also not given patentable weight. The instant claims are also drawn to compounds and compositions, while the co-pending claims are drawn to compositions; however, the formation of a composition from the same compounds would have been obvious to one of ordinary skill in the art. As the instant and co-pending claims are drawn to compositions comprised of the same compounds, they are not patentably distinct from each other.

***Claim Rejections-35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

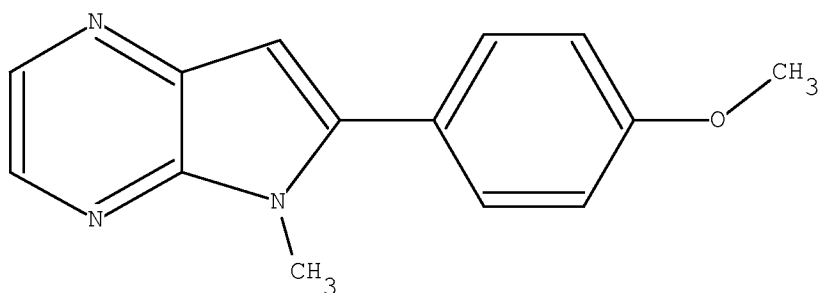
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

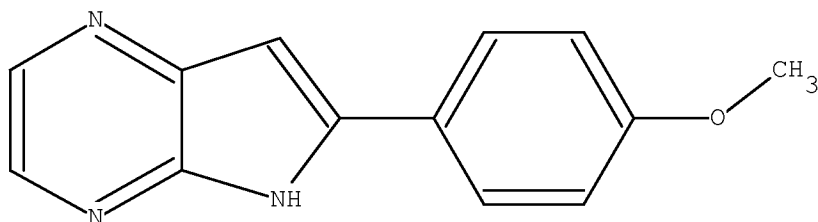
9. Claims 1-2, 4-7, 10-14, 15, 16, 17, 18, 19, 20-22, 23-25, 26-28, 29, 30, 31, 32, 33, 38, 39, and 41-46 are rejected under 35 USC 103(a) as being unpatentable over Davis et. al., *Tetrahedron*, **48**, pp. 939-952.



Claims 1-2, 4-7, 10, 14, 15, 16, 17, 18, 19, 22, 23, 24, 28, 29, 30, 38, 39, and 41-45 are drawn to the compounds of formula (I) and compositions, which includes the compound shown below:



Davis et. al. teaches the preparation of the compound shown below (Abstract; p. 941, compound (5); pg. 946, preparation paragraphs 4-5; p. 947, Table 3, item 14):

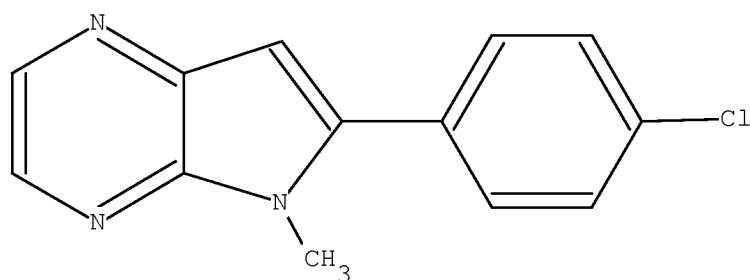


Davis et. al. also teaches that this compound is present in solvents, including ice-water (p. 946, preparation, paragraphs 4-5). The compound taught by Davis et. al. is nearly identical to the compound instantly claimed, with the exception that for the instantly claimed compound, the N atom of the pyrrolo ring is substituted with methyl; the compound taught by Davis et. al. has this position substituted with H. However, the replacement of hydrogen for a methyl group would have been prima facie obvious for one of ordinary skill in the art at the time of the invention, as these groups are obvious variants of each other. As Davis et. al. teaches that the compounds are present in a solvent carrier such as ice-water, Davis et. al. teaches that the compounds are present

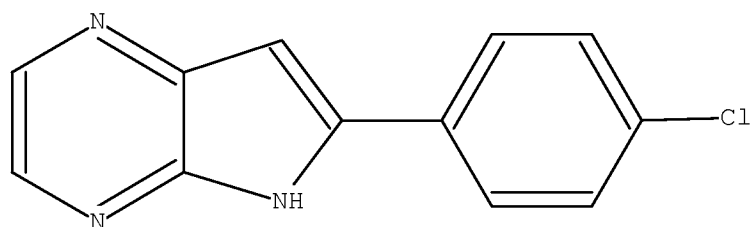
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in a composition. The instant claims are also drawn to compositions comprising the claimed compounds, with various dosages and routes of administration. However, as the claims are drawn to a composition, language which is drawn to dosages and routes of administration is intended use, and is not given patentable weight. Claim 39 also cites that the composition is for treating Alzheimer's disease; however, such language drawn to treatment in a composition claim is intended use, and is also not given patentable weight.

Claim 46 is drawn to the pyrazine compound of formula (I) shown below:



Davis et. al. also teaches that the compound shown below can be readily prepared (Abstract; p. 841, compound (5); p. 947, Table 3, item 15):

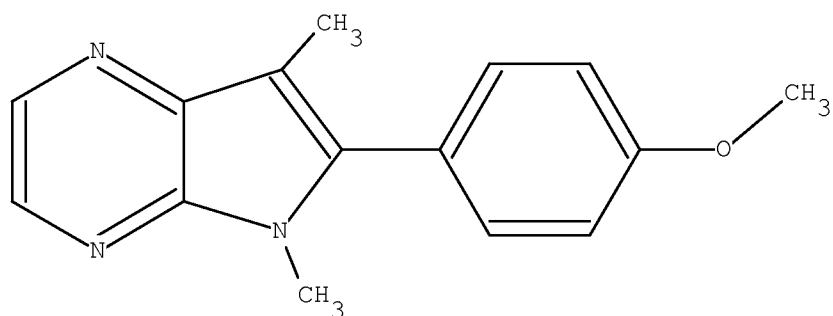


The compound taught by Davis et. al. is nearly identical to the compound instantly claimed, with the exception that the N atom of the pyrrole ring is substituted by hydrogen instead of a methyl group, as instantly claimed. However, as hydrogen and methyl substituents are obvious and homologous variants of each other, the substitution

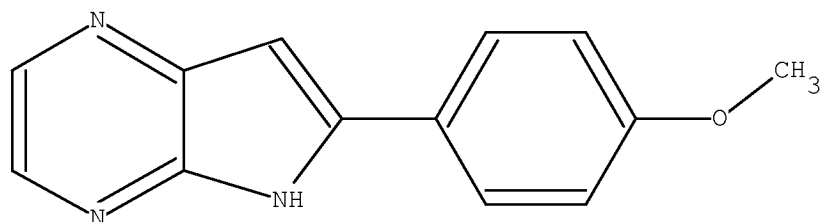
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of one group for another would have been prima facie obvious to one of ordinary skill in the art, at the time of the invention.

10. Claims 11-13, 20, 21, 25, 26, 27, 31-33 are drawn to compounds of formula (II), particularly the compound shown below:



Davis et. al. teaches that the compound shown below can be prepared (Abstract; p. 941, compound (5); pg. 946, preparation paragraphs 4-5; p. 947, Table 3, item 14):



The compound taught by Davis et. al. is structurally very similar to the compound instantly claimed. The compound instantly claimed has methyl group substituents present at the nitrogen atom and at position 7 of the pyrrolo ring; these positions are substituted by hydrogens for the compound taught by Davis et. al. However, the substitution of methyl groups for hydrogens would have been prima facie obvious for

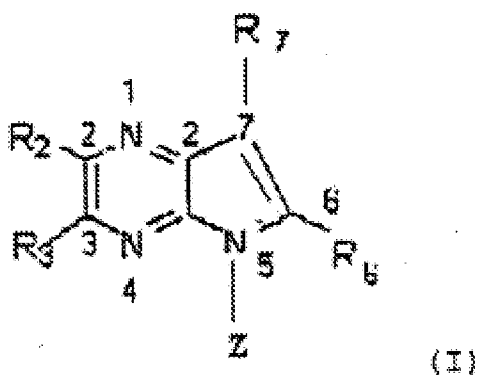
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one of ordinary skill in the art at the time of the invention, as these groups are obvious variants of each other.

***Claim Rejections-35 USC § 112***

11. Claims 1-4, 38-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 1 is drawn to pyrrolo-pyrazine compounds of formula (I) below:



The structure of formula (I) has a ring structure labeled as "7". The claim does not define what "7" is, and therefore, is indefinite. For purposes of searching for prior art and by searching for other compounds present in the claims, "7" was interpreted by the examiner as being a carbon atom. There are also two separate positions that are denoted as being of position "2" of the ring structure. As it is not certain which position Applicant is referring to as position "2", the claim is indefinite. As claims 2-4, and 38-46 are dependent claims of claim 1, they are also rejected.

Claim 1 also defines the position R<sub>6</sub> as “an optionally substituted aromatic cycle Ar”. However, claim 1 does not define what Ar is, and is therefore indefinite. For purposes of searching for prior art and by searching for other compounds present in the claims, “Ar” was interpreted as phenyl, naphthyl, furyl, thienyl, pyridyl, cyclopropyl phenyl, or phenyl dioxolyl, as further defined by claim 2.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST, with Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/  
Supervisory Patent Examiner, Art Unit 1617